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Research Paper

Comparative Diagnostic Value of Magnetic Resonance Spectroscopy and Pathology for Prostate Malignancy

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ABSTRACT

Background and Aim: Considering the non-invasiveness, sensitivity, and specificity of magnetic resonance spectroscopy (MRS), as well as its ability to diagnose prostate lesions in the early stages, this study aimed to determine the value of the MRS method compared to the standard method (pathology) for diagnosing prostate cancer.

Materials and Methods: This analytical cross-sectional study was conducted on 35 male patients. Individuals with indications for prostate biopsy were first subjected to a prostate-specific antigen (PSA) test and a finger examination. It should be noted that the negative or positive result of MRS, in terms of the imaging method used for the patients did not affect the biopsy. After evaluating the patients using the MRS method, the MRS and prostate biopsy results were assessed for each patient separately and compared with the pathological results of the biopsy. To determine the diagnostic value of the test, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.

Results: The sensitivity, specificity, positive, and negative predictive value of MRS in the left prostate region were calculated as 100%, 66.7%, 33.3%, and 100%, respectively. On the right side of the prostate, these values were 50%, 93%, 50%, and 93%, respectively. The diagnostic accuracy of MRS was 71.4% in the diagnosis of prostate cancer in the left area and 88.57% in the right area. On both sides, the test's sensitivity, specificity, and positive and negative predictive value were 87.5%, 59.3%, 38.9%, and 94.1%, respectively, and the diagnostic accuracy of neoadjuvant systemic therapy was 65.7%.

Conclusion: MRS, as a non-invasive method, demonstrates optimal sensitivity, specificity, and accuracy compared to other pathological and clinical methods.

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Introduction

Prostate cancer is the second most common cancer and the sixth leading cause of death in men. Research conducted in the field of cancer has increased the knowledge of experts and has helped identify the risk factors involved in the development and progression of this disease. It appears that this disease results from a complex interaction of various factors, including genetics, environment, culture, and lifestyle [1-3]. Despite the increase in the prevalence of this disease in recent decades, promising findings have been reported to reduce the mortality rate. The 5-year survival rate for most men with localized prostate cancer is about 100%, while it is 31% for the metastatic form. Additionally, the 10-year survival rate for all types of prostate cancer is about 98% [4, 5]. In addition to the biological nature of the disease, this low mortality rate has been largely affected by the optimization of diagnostic methods, and subsequently, effective and early therapeutic interventions. For example, the timely administration of effective treatments, such as abiraterone or docetaxel leads to optimal results in individuals newly diagnosed with metastatic prostate cancer [6]. Based on the available scientific evidence and considering the psychological and economic burden of the disease, it can be concluded that making a correct and quick decision regarding therapeutic interventions for prostate cancer is a key and unavoidable factor. On the other hand, the effectiveness of any type of treatment and the possibility of recurrence depend largely on proper risk classification and early diagnosis. Therefore, accurate and quick diagnosis is the most effective way to increase the survival rate and improve the quality of life for patients [5]. Existing approaches in the field of prostate cancer screening and diagnosis include measuring the serum level of prostate-specific antigen (PSA), digital rectal examination (DRE), trans-rectal ultrasound (TRUS), and biopsy.

These diagnostic methods have disadvantages, such as low specificity, low sensitivity, and invasiveness [7-10]. Magnetic resonance spectroscopy (MRS), as a practical method, enables non-invasive study by examining the levels of prostate metabolites, including citrate, polyamine, compounds containing choline, and creatine and phosphocreatine to detect cancer. It provides information about the prostate and its differentiation from other benign lesions [11]. Due to the non-invasiveness, sensitivity, and specificity of MRS, as well as its ability to detect small tumors in the early stages, it is considered a suitable method for diagnosing these types of diseases [12]. Therefore, the present study was designed to evaluate the MRS method in the diagnosis of prostate cancer in 35 Iranian men to determine whether the MRS method has suitable diagnostic value for the diagnosis of prostate cancer.

Materials and Methods

This cross-sectional analytical research was done on 35 men aged 40 to 80 years who were referred to Baqiyatallah Hospital between 2020 and 2021, with indications for prostate biopsy confirmed by the results of the PSA test. Before the biopsy, the PSA test was performed on the patients, and they underwent a finger examination [13]. It should be noted that the negative or positive result of MRS, in terms of the imaging method, did not affect the biopsy. The minimum sample size required for this study, based on Squillaci et al.'s study (29 people) [14], was 35. The inclusion criteria included Iranian ethnicity, an age range of 40 to 80 years, no metastatic cancer, and patients who were evaluated by PSA and DRE at Baqiyatallah Hospital confirming the need for biopsy. After obtaining the informed consent of the subjects according to the inclusion and exclusion criteria, the subjects were enrolled in the study.

In this study, MRS was performed as a multivoxel technique. The location of the voxels was determined using a 1.5 Tesla MRI (Siemens, Germany). The voxels were accurately placed in the desired location, and for the final diagnosis, the ratio of choline to creatinine was measured in that area [15]. Finally, to assess the diagnostic value of the test, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. The gold standard method considered was "pathology findings" based on prostate cancer. Since the results of biopsy tests for the right and left prostate regions of the patients were available separately, the diagnostic value was checked once for the left prostate region, once for the right region, and once without considering the region of malignancy. Finally, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated from biopsy and MRS data separately.

Results

Table 1 compares the MRS and biopsy results. Considering the biopsy result as the definitive diagnosis (standard diagnostic method) for the left prostate region, the sensitivity, specificity, and PPV and NPV of MRS, reflecting true and false positives and negatives, were 100%, 66.7%, 33.3%, and 100%, respectively. The diagnostic accuracy of MRS in the diagnosis of prostate

Table 1. Results of biopsy and MRS tests of the patients

MRS Results		No. (%)		Total
		Biopsy Results		
		Positive	Negative	
MRS of the right areas of the prostate	Positive	5(100)	0(0)	5
	Negative	10(33.3)	20(66.7)	30
MRS of the right areas of the prostate	Positive	2(50)	2(6.4)	4
	Negative	2(50)	29(93.6)	31

MRS: Magnetic resonance spectroscopy.

cancer in the left region was 71.4%. The results for the right side confirmed the ability of the MRS test to diagnose prostate cancer in the right region for patients with right-sided prostate cancer. The positive biopsy result for the right region was 50%. However, the ability of this test to detect healthy individuals when their biopsy results were negative was 93%93%. The PPV, which indicates the probability of having prostate cancer (left area) when the MRS result is also positive, was 50%. The NPV, which indicates the probability that a person is healthy when the MRS test result is also negative, was 93%. Finally, the diagnostic accuracy of the MRS test was 88.57% (Table 1).

Then, the general diagnostic value of the MRS method was investigated. In this approach, the left and right areas of the prostate are not separated for examination; if the disease is diagnosed as adenocarcinoma in one area of the prostate, it is considered adenocarcinoma (positive result). The results of prostate biopsy and MRS tests are presented in Table 2. The sensitivity, specificity, PPV, and NPV of the tests were 87.5%, 59.3%, 38.9%, and 94.1%, respectively, and the diagnostic accuracy of neoadjuvant systemic therapy (NAST) was 65.7%.

Discussion

Common methods have their limitations in the diagnosis of prostate cancer. For example, DRE misses up to 45% of all cancers that are detected later in follow-up biopsies. Additionally, cancers detected by DRE are at an advanced stage in 50% of cases. When using PSA, with a cutoff of 4 ng/mL as an indicator of prostate cancer, there is a probability of missing 25% of prostate cancers [16]. In addition, the PPV of the test in asymptomatic men is only 30% [17]. These results are consistent with the present study. MRI, when using an endorectal coil as a primary diagnostic tool, is not suitable for diagnosing prostate cancer due to its specificity and low PPV [18]. However, the specificity of MRI for staging in stages B and C is 77%, and it has a very high sensitivity for detecting tumors that have spread outside the prostate and seminal vesicles [19, 20].

To date, histopathological examination of biopsy tissue is the gold standard for the diagnosis of prostate cancer. However, this method yields only 50% sensitivity and 82% specificity. In these cases, malignancies are easily overlooked due to their multifocal and heterogeneous nature, which occurs in 85% of patients [21]. It has been reported that after radical prostatectomy, the results determined by biopsy have increased in 54% of patients [22]. MRS can identify the resonance spectrum of the chemical

Table 2. Results of prostate biopsy and MRS tests

Prostate MRS Results	No. (%)		Total
	Biopsy Results		
	Positive	Negative	
Positive	7(87.5)	11(40.7)	18
Negative	1(12.5)	16(59.3)	17

MRS: Magnetic resonance spectroscopy.

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composition of tissues, providing information related to both the chemical composition and metabolic characteristics of the tissues. Based on the inclusion criteria, this study evaluated the MRS method in the diagnosis of prostate cancer in a statistical population of 35 Iranian men.

Based on the results of the studies reviewed in a systematic review, the sensitivity of MRS in diagnosing prostate cancer and distinguishing it from benign lesions was estimated at 74.03%. Concerning the specificity of this diagnostic method, the results of the review of all studies indicated an average value of 74.27%. In general, the accuracy of MRS has been calculated at 77.26% [23]. In this study, the sensitivity and specificity of MRS were 100% and 66.7%, respectively. This difference may be due to the types of studies and the forms of screening used. It should be noted that in the systematic review study, the estimation from 21 studies was prospective; however, no significant difference was observed, and the findings can be considered in the same direction. We found that there was heterogeneity of non-threshold effects in sensitivity and specificity among the studies. In subgroup and meta-regression analyses, it was shown that the covariates "type of data collection" and "whether the study was conducted in a developed country" may be potential sources of heterogeneity concerning sensitivity [24] In normal prostate tissue, high levels of citrate are found. Therefore, the MRS imaging method of tumors is based on increasing the choline + creatine/citrate ratio [21]. In some studies, detected voxels are determined by biopsy sites. However, biopsy is inaccurate because prostate cancer is multifocal and heterogeneous, and is limited in its ability to examine all cancers, sites, and grades [22]. Hence, their positive results [25, 26] are much smaller than the negative results, and the sensitivity is not reliable.

Based on the study by Zakian et al. [27], which investigated MRS imaging and the ratio of the sum of choline and creatine to citrate, a positive correlation was observed between pathological results and Gleason grading. The data from this study show that in the diagnosis of cancer with a Gleason grade of 3+3, MRS tumor imaging has a sensitivity of 44.4%, and in cancer with a Gleason grade of more than 8, the sensitivity is 89.5%. Therefore, a high proportion of tumors with a Gleason grade of six and lower do not show abnormal metabolite ratios in the voxel. The results showed that the total choline + creatine/citrate ratio had a significant relationship with the stage of cancer; the greater the stage of cancer, the higher the total choline + creatine/citrate ratio. In this regard, Yu et al.'s study involved a combination of endorectal MRI and MRS performed on nine young volunteers, five patients with benign prostatic hyperplasia (BPH), and 85 patients with prostate cancer and BPH. The results of MRI and MRS in these patients were compared with the histological findings after the operation and showed that the total choline + creatine/citrate ratio in the cancerous areas was significantly different from its values in the surrounding normal prostate tissues [25]. Other studies have also indicated that spectroscopic examination and the use of the total choline + creatine/citrate ratio can be an acceptable index for prostate cancer diagnosis [28, 29].

Conclusion

As our findings and other studies indicate, the effectiveness of MRS alone in diagnosing and excluding primary care is limited. MRS alone cannot confirm or rule out malignancy. The combination of other data and clinical tests (such as cholinesterase levels) is necessary to differentiate inflammation from cancer or hyperplasia, which requires a comprehensive analysis. Considering that such studies are specifically related to imaging technology, it can be expected that the previous studies using devices with older technology will be less accurate for MRS, while future studies will likely be more accurate.

Ethical Considerations

Compliance with ethical guidelines

All steps and the implementation process of this study were carried out after receiving approval from the Research and Technology Vice-Chancellor of Baqiyatallah University of Medical Sciences and its Ethics Committee (Code: IR.BMSU.BAQ.REC.1400.038).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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